Tumour lysis syndrome in a patient with metastatic melanoma treated with biochemotherapy

Sir,

Tumour lysis syndrome (TLS) may complicate the treatment of highly proliferative, chemosensitive haematological malignancies [1]. Rapid cell death is associated with hyperuricaemia, hypocalcaemia, hyperphosphataemia, and hyperkalaemia [2]. Acute hyperuricaemic nephropathy (AHN) arises from precipitation of uric acid crystals within renal tubules and subsequent uptake into tubular epithelial cells, thereby promoting tubular necrosis and acute renal failure [3]. An emergence of TLS in solid tumour malignancies might be expected with improvements in therapy [4]. We report the rare occurrence of TLS with AHN in a patient with metastatic melanoma treated with a combination of chemotherapy and immunotherapy.

Case. Three years after surgery for cutaneous melanoma, a 41-year-old male presented with symptomatic relapse. Computed tomography demonstrated multiple lesions in the liver and gastro-intestinal tract. Histological confirmation of melanoma was obtained from a duodenal biopsy. The patient received a 5-day course of biochemotherapy (cisplatin 30 mg/m² and dacarbazine 250 mg/m² on days 1–3 of treatment, and interferon-alpha 10 MU/m² on days 1–5 of treatment). Progressive oliguria developed within 2 days of commencing treatment, and there was worsening of ascites and peripheral oedema. Central venous pressure measurements were satisfactorily maintained throughout. Serum creatinine rose from day 4 of treatment, reaching a value of 820 μmol/l on day 10. Other results were as follows: haemoglobin 7.6 g/dl, white cell count 5.9×10⁹/l, platelets 28×10⁹/l, sodium 129 mmol/l, potassium 3.6 mmol/l (with combination diuretic therapy), bilirubin 23 μmol/l, ALT 30 IU/l, ALP 496 IU/l, albumin 28 g/l (with albumin infusions), calcium 1.8 mmol/l (2.2–2.6 mmol/l), magnesium 1.03 mmol/l (0.7–1.0 mmol/l), phosphate 2.24 mmol/l (0.8–1.3 mmol/l), urate 0.94 mmol/l (0.2–0.45 mmol/l). Ultrasonographic examination showed no evidence of extrarenal obstruction or caval or renal-vein thrombosis. Haemodialysis was initiated to allow an assessment of biochemotherapeutic response, but the patient’s general condition deteriorated during the first week of treatment and renal support was discontinued at his own request.

Comment. The combination of allopurinol (a xanthine oxidase inhibitor) and sustained alkaline diuresis constitutes an effective prophylactic regimen for anticipated AHN and is therefore an essential component of treatment protocols for haematological malignancies such as leukaemia and lymphoma. Malignancies such as metastatic melanoma are relatively chemoresistant and AHN prophylaxis is not routine in clinical practice. However, new biochemotherapeutic regimens for metastatic melanoma have been shown to achieve more effective tumour regression [5]. AHN has been reported in two patients, one receiving a combination of standard chemotherapy and immunotherapy (interferon-alpha and interleukin-2), and another receiving tumour necrosis factor-alpha and anti-GD3 ganglioside monoclonal antibody [4,6].
Several factors may have contributed to the development of acute renal failure in this case, but with early hypocalcaemia, hyperphosphataemia, and hyperuricaemia it is likely that AHN played a significant role. The absence of hyperkalaemia may be explained by the continual use of loop and thiazide diuretic therapy. Cisplatin nephrotoxicity is typically non-oliguric with a more delayed onset. Hypomagnesaemia, also a common feature of cisplatin nephrotoxicity, did not occur in this case [7].

We wish to increase awareness of AHN as a complication of cytoreductive treatment for patients with large solid tumours. Renal dysfunction may be compounded by the inherently nephrotoxic effects of biochemotherapeutic regimens. Prophylaxis for AHN will help to ensure that the potential benefits of new treatments are not offset by preventable renal complications.

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